Remarks

Claims 1-18 are pending. Claims 6-16 and 19 have been withdrawn. Claims 1-5, 17-18, and 20 are currently under examination.

Rejection under 35 U.S.C. § 102

Claims 1- 4, and 17-18 are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Perryman et al. The Examiner states that Perryman et al. discloses antibodies specific to *C. parvum* sporozoites.

Applicants previously argued that the antigen of Perryman et al. is described as p23 (p. 6, line 30 and p.13, lines 11-12). This is the same 23 kD antigen discussed in reference to Moss et al., which was previously cited as prior art. The p23 antigen is not specific to sporozoites. Bonafonte et al. (Exp. Par., 96: 32-41, 2000, previously provided) disclose that the 23 kD antigen of *C. parvum* "is present in both the sporozoite and merozoite stages." (p. 33, left col. 2nd par.) As previously discussed, the claims state that the antibody is "specific for a soluble antigen of a *C. parvum* sporozoite." Because the 23 kD can be obtained from merozoites, it is not specific to sporozoites.

The Examiner has stated that this argument is not persuasive because, "There is no clear evidence that the antigen to which the antibody binds, taught by Perryman, and the antigens taught by Moss and Bonafonte are the same. Thus the argument that this antigen is not specific to sporozoite is not persuasive." Applicants respectfully traverse. There is clear evidence that antigens are the same. Bonafonte et al. state that:

> Fig. 1 demonstrates specific reactivity of anti-*Crytosporidium* polyclonal antibodies with proteins of ~23 kDa (cleaved protein [Cp23])... The Cp23 sequence which codes for an 11.2-kDa protein (Perryman *et al.,* 1996) has been shown on SDS-gels and Western blots to migrate as a 27-kDa (Priest et al., 1999; Perryman *et al.,* 1996) or 23-kDa (Perryman *et al.,* 1996) protein, depending on the gel conditions.

The paper referred to in Bonafonte et al. as "Perryman *et al.*" is attached as Exhibit A (Perryman et al., Mol Biochem Parasitol., 1996 1;80(2):137-47.) The 23 kDa protein referred to in Perryman et al. (1996) is the same as that referred to in the Perryman et al. reference currently cited as prior art (WO 98/07320). Perryman et al. (1996) disclose that the p23 peptide has the amino acid sequence QDKPADAPAAEAPAAEPAAQQDKPADA (p. 140, right col.) and Perryman et al. (WO 98/07320) disclose the same sequence in SEQ ID NO: 4 as p23 (see sequence listing, as well as claims 1-2). As disclosed above, Bonafonte disclose that the 23 kD antigen of *C. parvum* "is present in both the sporozoite and merozoite stages." (p. 33, left col. 2nd par.) This is clear evidence that the antigen taught by Perryman et al. (WO 98/07320) is the same as that taught by Bonafonte et al. and Moss et al. Therefore, applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 1- 4, and 17-18 are rejected under 35 USC 102(b) as allegedly being anticipated by Petersen et al. The Examiner states that Petersen discloses monoclonal antibodies to a soluble *C. parvum* sporozoite glycoprotein.

Applicants respectfully traverse. Previously, applicants stated that Petersen et al. discloses antibodies that are reactive with a >900,000-M *C. parvum* sporozoite glycoprotein known as gp900. However, Bonnin et al. (Parasitol. Res., 87:589-592, 2001, previously

provided) discloses that gp900 is "an abundant glycoprotein of *C. parvum* merozoites and sporozoites." (Abstract.) Therefore, the antibodies directed against gp900 would not have been specific for a *C. parvum* sporozoite, as they would have also been directed against merozoites.

The Examiner argues that this argument is not persuasive because, "though Petersen has shown that some of the antibodies cross reacts with merozoite antigens, Petersen is silent with respect to the cross-reactivity of the monoclonal antibody designated E6. Thus, it is concluded that the antibody E6 recognizes an epitope that is unique to gp900 found in sporozoites. Absent evidence to the contrary, the antibody taught by Petersen is seen to be the same as the instant claim." (p. 10 of the Office Action.)

However, gp900 is a protein found in sporozoites *and* merozoites. There is no scientific basis to assert that any antibody directed to gp900 is specific for sporozoites. The statement that "the antibody E6 recognizes an epitope that is unique to gp900 found in sporozoites" is not correct, as there is no data to support that there are epitopes of gp900 found in sporozoites but not in merozoites. The Examiner has shown no distinguishing properties between gp900 obtained from one versus the other. It is the same protein, regardless of where it is found. Therefore, any antibody directed against it is, by nature, directed against sporozoites *and* merozoites, and therefore not specific for sporozoites.

Furthermore, in order to be a proper rejection under 35 USC 102(b), "the reference must teach every aspect of the claimed invention either explicitly or impliedly. Any feature not directly taught must be inherently present." (MPEP, 706.02(a)). As stated above, there is no data

to support that there are epitopes of gp900 found in sporozoites but not in merozoites. Therefore, Applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 1- 4 and 17-18 are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Riggs et al. The Examiner states that Riggs et al. discloses compositions comprising monoclonal antibodies to *C. parvum* sporozoites.

The Riggs et al. reference discloses five MAbs that were found to give a posteriorly capped staining on sporozoites with posteriorly extruded fluorescent material, suggesting the presence of shed antigens. However, Riggs et al. also discloses that "these [five] MAbs were found to bind to oocyst walls." (page 7, lines 20-24). Applicant previously argued that these monoclonal antibodies are not specific for sporozoites, as they also bind oocyst walls.

The Examiner argues that "Since Riggs discloses that 112 hybridomas were found to positively bind to sporozoite as antigenic targets, and 5 were found to also bind to oocyst wall, this represents a small proportion of the antibody composition that react with a cross-reactive antigen, therefore, the composition is considered to have specificity for the target antigen, i.e., sporozoite." (Pages 11-12 of Office Action.)

Applicants would like to point out that, first of all, the 112 hybridomas were found in a *preliminary* assay to have specificity for GP25-200. This protein, however, is described as heterogenous, and therefore cannot be considered to be specific for sporozoites. In regard to GP25-200, Riggs et al. states that: "immunoreactive beads in immunoaffinity purified antigens comigrated with bands of similar molecular weight derived from whole organisms... As a result of the size heterogeneity, the antigen recognized by the C4A1 mAb has been referred to as the

'GP25-200' complex." (Page 6, lines 4-7.) Therefore, this antigen could have also been derived from whole organisms, and was therefore not specific for sporozoites.

The Examiner stated that "Riggs discloses that 112 hybridomas were found to positively bind to sporozoite as antigenic targets, and 5 were found to also bind to oocyst walls." However, this is not a correct characterization of the experiment performed. As described above, the 112 hybridomas were identified in a "preliminary indirect immunofluorescence assay" (p. 6, line 25.) In a subsequent assay, "five of the mAbs tested in the live indirect immunofluorescence assay were found to give a posteriorly capped staining pattern on sporozoites with posteriorly extruded fluorescent material... Additionally, these mAbs were found to bind oocyst walls." (Page 7, lines 20-25). Therefore, not all 112 hybridomas were tested for specificity to sporozoites and only five found to bind oocyst walls. Instead, the five that were found to give a posteriorly capped staining pattern on sporozoites were also found to react with oocyst walls. Therefore, all five antibodies that reacted with sporozoites also reacted with oocysts walls, and therefore, none of them can be considered to be specific for sporozoites. Applicants respectfully request reconsideration and withdrawal of this rejection.

Pursuant to the above remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of the application to issue.

A Credit Card Payment Form PTO-2038 authorizing payment in the amount of $450.00, representing the extension of time fee is enclosed. This amount is believed to be correct;

however, the commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8

I hereby certify that this correspondence, including any items indicated as attached or included, is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date indicated below.

Janell T. Cleveland — Date 7/26/05